DOI:
10.1016/j.coph.2015.03.003

Document Version
Peer reviewed version

HOW BEST TO MEASURE COUGH CLINICALLY

Review article

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Keywords: cough, quality of life, cough monitors, capsaicin, endpoints

Manuscript word count: 1664

Abstract

It is possible to measure cough by assessing its severity, frequency, intensity, associated urge and its impact on quality of life. Cough severity can simply be assessed with a Visual Analogue Scale. Cough frequency can be assessed objectively with cough frequency monitors. Validated cough monitors include the Leicester Cough Monitor and the VitaloJAK. Cough reflex sensitivity measurement is better used to investigate the mechanisms of action of antitussive medications, rather than assessing efficacy. Health-related quality of life measures are available to assess the impact of cough; they include the validated Leicester Cough Questionnaire and Cough-specific Quality of Life Questionnaire for adult patients. It is best to assess cough with a combination of subjective and objective tools, to capture its wide-ranging impact.

Introduction

Cough is one of the most common reasons why patients consult their doctor. Cough can lead to significant physical, psychological and social morbidity [1]. Adverse symptoms associated with cough such as incontinence and pain, absence from work and social embarrassment are frequent [2]. Cough should be measured and quantified when objective verification is necessary and for assessing the efficacy of therapy [3]. The formal assessment of cough is mostly limited to the research setting, since in the clinic most physicians simply ask patients about the severity of their cough. However, validated subjective and objective tools are available, such as cough frequency monitors and Health-Related Quality of Life (HRQOL) questionnaires [4]. This review will focus on recent developments in the assessment of adult patients with cough.

Which tool to assess cough?

The choice depends on the context of the setting. Several components of cough can be assessed, which include severity, frequency, intensity, urge and its impact (HRQOL), see Figure 1. The most widely used tools assess severity, frequency and HRQOL. In the clinic, when the doctor asks the patient about their cough, the impact of cough on the individual can easily be overlooked. The 0-10 cough severity rating is one simple measure that could be used in a busy clinic. The clinician asks the patient to rate the severity of their cough between 0 and 10 and this is simple to document within the consultation notes. This may have the advantage of giving the clinician a better perspective about the severity of cough and facilitate longitudinal observation. Moreover, it improves the communication between clinicians about the severity of cough. Another simple, but more formal tool is the cough Visual Analogue Scale (VAS), which can be a paper or electronic format. VAS as well as

HRQOL questionnaires are the most commonly used outcome measures in research, and can easily be applied to clinical practice.

Objective quantification of cough is perhaps more important in the evaluation of antitussive therapy. Cough frequency monitors are being increasingly used in clinical trials [5]. The urge to cough can be assessed subjectively during spontaneous or induced cough. It has largely been assessed in studies investigating mechanisms of cough [6]. Further studies are required to investigate the potential of urge to cough as a clinical end-point in the evaluation of antitussive therapy. The intensity of cough can be assessed objectively with physiological measures such as cough flow, electromyography and oesophageal (thoracic) pressure. Some of these techniques are invasive and a continuous ambulatory recording in the patients' environment is not yet possible. Physiological measures of cough are limited to the laboratory setting [7].

The concept that the subjective assessment, objective cough challenge and cough counting reveal different facets of the clinical cough is important. The interpretation of their findings is entirely dependent on the question asked. From the patients' perspective, subjective assessment and impact on HRQOL is important. The number of coughs is not something patients report to their physician. Cough counting is however important when evaluating the efficacy of an antitussive medication in a clinical trial. They can be useful to demonstrate efficacy objectively since subjective measures could potentially be influenced by other factors, for example, drugs that act centrally with a potential to affect mood. The relationship between the three methodologies has been studied in detail by Faruqi et al [8]. Cough counts were only moderately associated with subjective assessments and cough challenge tests. Cough counts related marginally better with HRQOL than cough severity VAS. This data

suggests the three methods assess different aspects of cough. A combination of subjective and objective tools is necessary to assess cough comprehensively but the choice of tools should be based on the question being asked.

Cough Severity

Cough severity can be assessed with the cough VAS, the Cough Severity Score (CSS) and the Cough Severity Diary (CSD). Cough VAS is a brief, simple and cost-effective measure of cough severity [9]. It is important to ensure that the scale is 100 mm in length, especially when electronic scales are used. The scale must be closed at both ends with perpendicular lines, and the wording at the extremes of the scale must be stated outside the scale. An example of a cough VAS is given in Figure 2. VAS has not been validated by the rigorous methodology applied to other subjective measures, such as HRQOL questionnaires. In the author's opinion, reliability, repeatability and responsiveness are likely to be very good, but this requires formal investigation. The minimal clinically important difference (MID) of the VAS in acute cough has been reported to be 17 mm [10].

The Cough Severity Score (CSS) is another subjective tool. It is a two-part question relating to cough symptoms during the day and night [11]. The response scale captures some aspects of cough frequency, intensity and overall impact. The CSS still requires further validation and its MID has not been reported. The Cough Severity Diary (CSD) is a seven-item questionnaire that asks patients about the severity, intensity and impact on quality of life [12]. There is little published evidence regarding this tool and the MID has not been reported.

Quality of Life Questionnaires

There are two HRQOL questionnaires widely used in the assessment of adult patients with cough. The Leicester Cough Questionnaire (LCQ) is a nineteen-item questionnaire that comprises of three health domains; physical, psychological and social [13]. It has been evaluated in patients with chronic and acute cough, post-infectious sub-acute cough, bronchiectasis and chronic obstructive pulmonary disease (COPD) [10, 14-17]. The LCQ has been well validated. Its internal consistency, repeatability and responsiveness have all been reported [13, 18, 19] and the MID is 1.3 and 2.0 in chronic and acute cough respectively [10, 19]. The LCQ has been used in clinical trials as an outcome measure [20, 21]. The Cough-specific Quality of Life Questionnaire (CQLQ) is another well-validated HRQOL questionnaire [22]. This tool was developed in the United States and consists of twenty-eight items allocated to six domains. The CQLQ has been validated in acute and chronic cough. Its internal consistency, repeatability and responsiveness have been reported. The MID is 13 units in chronic cough [23]. The CQLQ has also been utilised in clinical trials evaluating antitussive therapies [24].

Objective Cough Frequency Monitoring

For the objective assessment of cough frequency, there are two tools currently in use in clinical trials, the Leicester Cough Monitor (LCM) and the VitaloJAK. They are both ambulatory and measure cough in the patient's own environment. The LCM is an automated monitor [25-27]. It consists of an MP3 recording device and a lapel microphone. It can record up to four days continuously and it is practical for large-scale, multi-centre studies due to its automated capability. The cough detection software is based on the Hidden Markov model, a method used in speech recognition. The LCM detects cough events whether occurring in isolation or in a bout. The LCM has been validated [5, 25, 28] and utilised in patients with

chronic cough, acute cough and COPD [10, 28]. This tool has been used to evaluate antitussive therapies in randomised clinical trials [21].

The VitaloJAK also consists of an MP3 recording device, but has two microphones, a contact and a lapel microphone [29]. It can record patients for 24 hours in an ambulatory setting. In contrast with the LCM, cough is counted by trained technician from condensed recordings. The VitaloJAK has been validated, and been used in patients with acute cough, chronic cough and COPD. It has also been used to evaluate antitussive therapy in clinical trials [30, 31].

Cough Reflex Sensitivity Challenge Tests

The sensitivity of the cough reflex can be evaluated by numerous tussive agents, most commonly capsaicin and citric acid. Other tussive agents available include fog, low chloride solutions, bradykinin, prostaglandin E2, mannitol and cinnamaldehyde. The most widely used methodology is sequential single breath inhalations with a dosimeter to establish the concentration of tussive agent causing two and five coughs (C2 and C5 respectively) [32, 33]. Cough reflex challenge tests are valuable tools to study pharmacokinetics and interrogating cough receptor interaction [34]. The limitations of cough challenge tests are that they cannot be used as diagnostic tests because they do not discriminate healthy subjects from patients with cough. Additionally they cannot be used to measure the severity of cough as they do not reflect symptom burden [35]. Recently, a capsaicin challenge test that involves measuring the Emax, which is the maximum cough response evoked by any concentration of capsaicin, has been reported to discriminate healthy subjects from those with cough better than the standard methodology [36]. An important difference to the standard methodology is that Emax involves four inhalations of capsaicin at each dose. Whilst this is a promising development, the discrimination between healthy and cough subjects with Emax seems to be applicable

only when comparing population means and the discriminative value is likely to be lower when evaluating individual patients. Emax needs to be evaluated in larger numbers of subjects to confirm the findings of this preliminary study. A tidal breathing method delivering capsaicin has also been reported to discriminate patients with cough well from healthy controls [37]. C5 was superior than C2 for this purpose. Other methods of performing and analysing cough challenge tests should also be explored for diagnostic use. The urge to cough following inhalation of capsaicin is a potential method.

Conclusion

There are numerous validated tools available to assess cough. A combination of subjective and objective measures is desirable. In a clinical setting the severity of cough can easily be assessed by asking the patient to rate it on a scale between 0-10. In clinical trials of antitussive medications objective measures such as cough frequency monitors are being increasingly used as primary endpoints. They should always be accompanied by secondary outcome measures assessing symptom severity and HRQOL. HRQOL is perhaps the most important endpoint from a patient's perspective. Further work needs to be done to develop and evaluate measures of cough intensity and urge to cough.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:
* of special interest
** of outstanding interest

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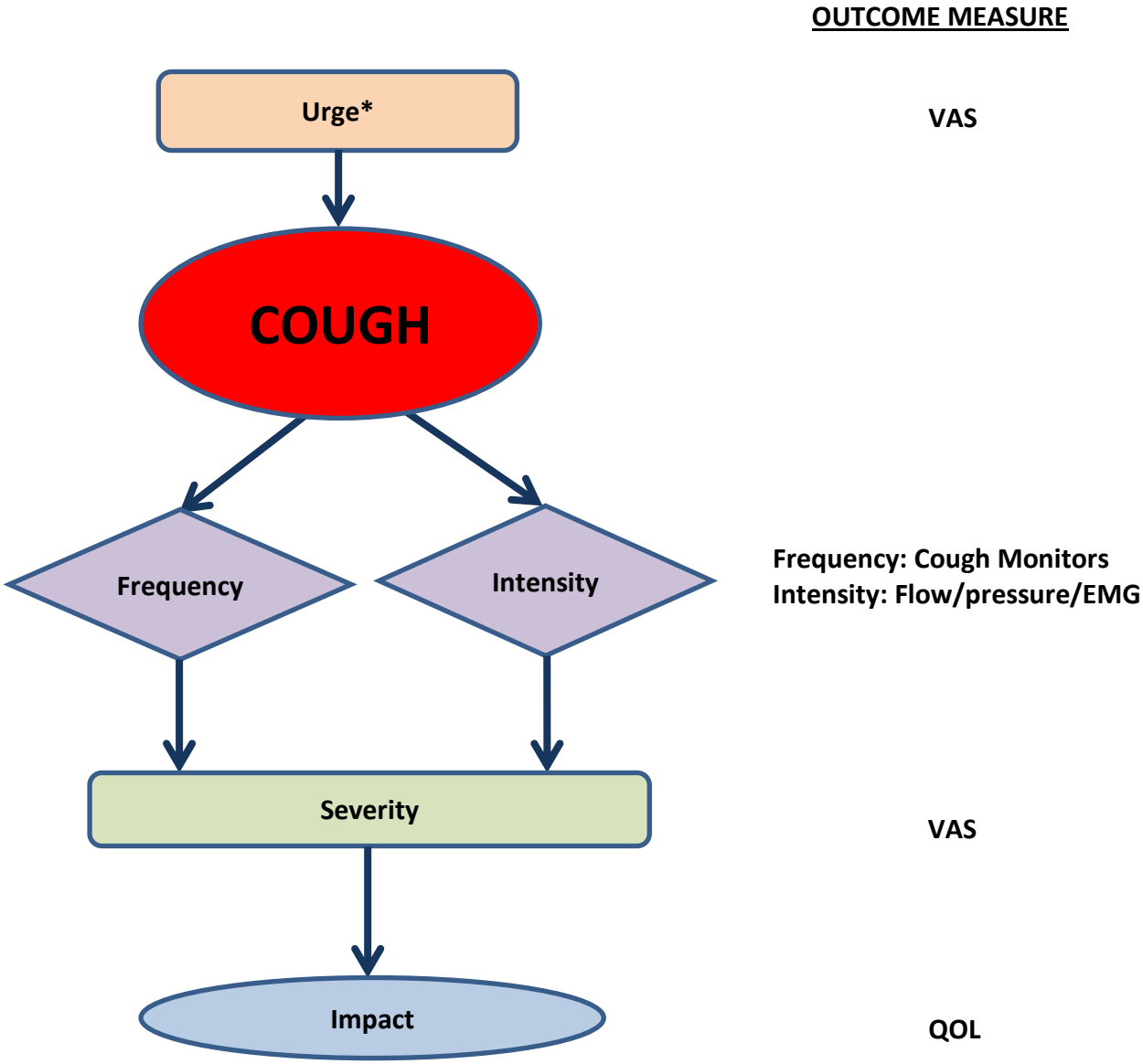
Table of figures

Figure 1. Measuring cough.

Figure 2. Cough Severity Visual Analogue Scale.

Figure 1. Measuring cough.

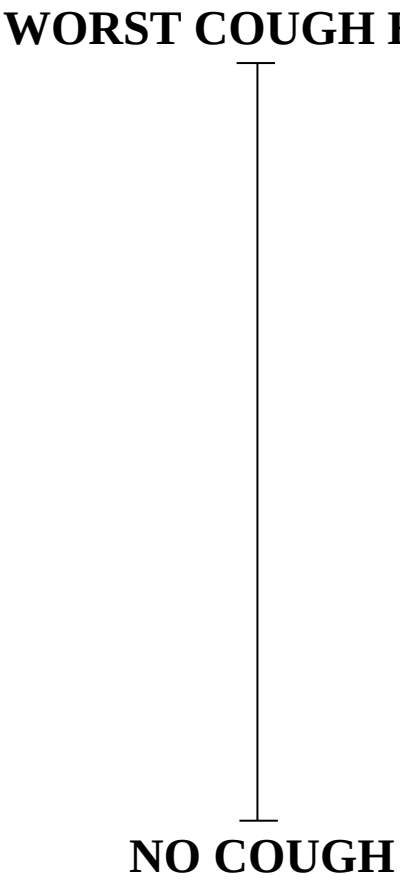


*Urge may be absent.

VAS: visual analogue scale; EMG: electromyography; QOL: quality of life.

Figure 2. Cough Severity Visual Analogue Scale.

Please put a cross on the line to indicate the severity of your cough in the past 2 weeks.



Note this scale may not be to size (100 mm).